REMARKS

The Claimed Invention

The claimed invention is directed to antigen presenting vesicles.

The Pending Claims

Prior to entry of the above amendments, Claims 13-17 are pending.

The Office Action

Claim 17 is withdrawn.

Claims 13-16 are rejected under 35 USC § 102(b)

Claims 13 and 15 are rejected under 35 USC § 102(b)

Amendments

Cancel Claims 15 and 17 and add new Claim3 18-20.

Support for the amendments to the claims and for new Claims 18-20 can be found, for example, on page 2, lines 21-24

No new matter is introduced by the amendments and the Examiner is respectfully requested to enter them

Response to the objections and rejections

In the response that follows, the Examiner's individual rejections are provided in full text, as identified by indented small bold print, followed by Applicant's response.

Election/Restriction

3. Claim 17 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic of linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12, filed July 3, 2000.

Claim 17 is drawn to vesicles comprising both MHC class I and MHC class II molecules. However, applicant elected vesicles comprising MHC class II molecules and it was explained in the

Office Action mailed August 14, 2000 that MHC class I and MHC class II peptides are processed via separate pathways.

Accordingly, claims 13-16 are the subject of examination in the present Office Action.

Claim 17 has been cancelled.

35 U.S.C. 102(b) Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country more than one year prior to the date of the application for patent in the United States.

4. Claims 13-16 are rejected under 35 USC § 102(b) as being anticipated by Harding et al. (J. Immunology, 151:3988-3998, 1993, of record).

Harding teaches the subcellular fractionation of murine peritoneal macrophages to produce lysomal fractions containing MHC Class II molecules (see entire article, especially page 3990, column 2, last 2 paragraphs in particular), and that fractions containing lysosomes and light density membranes contained peptide-MHC-II complexes that were detected by T cells, (see entire article especially page 3992, column 1, last paragraph in particular). Harding teaches the differential centrifugation of the membrane-containing fractions over a Percoll gradient at 100,000 x g, which is greater than the 70,000 x g recited in claims 14 and 16 and will pellet out all material obtainable at 70,000 x g. Harding teaches that B cells, another type of antigen presenting cell, comprise similar compartments (page 3997, second column in particular). The prior art teaching anticipates the claimed invention.

5. Claims 13 and 15 are rejected under 35 USC § 102(b) as being anticipated by Amigorena et al (Nature, 369:113-120, 1994, of record).

Amigorena teaches the subcellular fractionation of a B cell line to produce fractions containing membrance vesicles with MHC Class II molecules (see entire article, especially page 115, column 2, last paragraph in particular), which contained processed peptide (see entire article, especially page 118, first paragraph of the Discussion Section in particular). The prior art teaching anticipates the claimed invention.

The above rejections are believed avoided in part by amendment of the claims and are traversed in part because neither of the identified prior art documents discloses or

suggests an antigen presenting vesicle released into the extracellular milieu by a B lymphocyte. Prior to Applicants invention, it was not known that B cells release vesicles extracellularly, and that these vesicles therefore can be isolated and used as immunogens.

According to the Examiner, Harding teaches the subcellular fractionation over a Percoll gradient at 100,000 x g of murine peritoneal macrophages to produce lysosomal fractions containing MHC Class II molecules and suggests that B cells comprise similar [lysosomal] compartments.

Applicants draw the Examiner's attention to page 3992 (right column, last sentence of the 2nd paragraph) of Harding et al. which states that "*peptide-MHC-II complexes appeared first at high levels in lysosomes and later accumulated on the plasma menbrane*". Furthermore, pages 3993 (end of right column) and 3994 specify that "*lysosomal MHC-II molecules represent an intermediate population along the class II Ag processing pathway that is destined for later expression on the plasma membrane*" (emphasis added). The fractions analysed in this study are subcellular fractions. Lysosomes, prelysosomes and late endosomes are mentioned without being clearly distinguished (*see* end of page 3996 and beginning of page 3997)l there is nothing relating to vesicles released into the extracellular milieu by macrophages or other cells.

The document also states that "*Further work is necessary to understand in greater detail the transport relationships of this* [lysosomal] *compatrment with other endosomal and lysosomal compartments*" (page 39997, end of the first paragraph, right column). The authors hypothesize "*that MHC-II is first transported to the plasma membrane and then internalized to target through endosomes to lysosomes"* (Page 3997, second paragraph,right column). Contrary to the claimed invention, lysosomes (versus vesicles) described in said document, may only be isolated by cellular fractionation and are not released into the extracellular millieu by the producing cells.

According to the Examiner, Amigorena teaches the subcellular fractionation of a B cell line to produce fractions containing membrane vesicles with MHC Class II molecules which contained processed peptide. Applicants stress that this reference

relates exclusively to the transport of class II molecules to the plasma membrane through the Golgi (*see* for example page 117 of Amirogena et al.). Again, the described vesicles are considered as "*intermediates in the intracellular transport*" of MHC class II molecules (page 118, right column). Secretion or release of the vesicles is never mentioned or even suggested. The invention results from the totally unexpected discovery that B cells release vesicles, that such vesicles can be isolated, and that these vesicles exhibit high immunogenic properties. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

CONCLUSION

In view of the above amendment and remarks, it is submitted that this application is now ready for allowance. Early notice to that effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (831) 648-3090 X103.

Respectfully submitted,

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